WEST Search History

DATE: Wednesday, November 20, 2002

Set Name side by side	Query	Hit Count	Set Name result set
DB=USPT,PGPB,JPAB,EPAB,DWPI,TDBD; PLUR=YES; OP=OR			
L14	L10 and (array adj3 immobiliz$4 adj4 probe)	8	L14
L13	L12 and DNA	494	L13
L12	L10 and probe adj4 array	494	L12
L11	L10 and array	2341	L11
L10	L9 and hybrid$6	4189	L10
L9	L7 and hybridization	4253	L9
L8	L6 and double stranded	49207	L8
L7	L6 and protein adj4 bind$5	4593	L7
L6	L5 and transcription adj4 factor	5581	L6
L5	L4 and probe	27212	L5
L4	library	78411	L4
L3	L2 and Library adj3 (transcription adj3 factor adj3 probe)	0	L3
L2	L1	203	L2
DB=USPT; PLUR=YES; OP=OR			
L1	activated adj4 transcription adj4 factor	203	L1

END OF SEARCH HISTORY

```
=> d his

     (FILE 'HOME' ENTERED AT 13:44:50 ON 20 NOV 2002)

     FILE 'CA' ENTERED AT 13:44:54 ON 20 NOV 2002
L1           430 S ACTIVATED TRANSCRIPTION FACTOR#
L2           388 S L1 NOT 2002/PY
L3             5 S L2 AND LIBR?

=> s l2 not l3
L4           383 L2 NOT L3

=> s l4 and libr?(2w)(double stranded or ds)(5w)(DNA or nucleotide)
          72626 LIBR?
         371243 DOUBLE
          43837 STRANDED
          25378 DOUBLE STRANDED
                   (DOUBLE(W)STRANDED)
          45311 DS
         565131 DNA
         297214 NUCLEOTIDE
              6 LIBR?(2W)(DOUBLE STRANDED OR DS)(5W)(DNA OR NUCLEOTIDE)
L5            0 L4 AND LIBR?(2W)(DOUBLE STRANDED OR DS)(5W)(DNA OR NUCLEOTIDE)

=> s l1 and biolog?(5w)sample
        2861304 BIOLOG?
         513646 SAMPLE
            559 BIOLOG?(5W)SAMPLE
L6            0 L1 AND BIOLOG?(5W)SAMPLE

=> s l4 and libr?(w)ds(2w)DNA
          72626 LIBR?
          45311 DS
         565131 DNA
              0 LIBR?(W)DS(2W)DNA
L7            0 L4 AND LIBR?(W)DS(2W)DNA

=> s l5 step
L8   (    72626)LIBR?
L9   (   371243)DOUBLE
L10  (    43837)STRANDED
L11  (    25378)DOUBLE STRANDED
                   (DOUBLE(W)STRANDED)
L12  (    45311)DS
L13  (   565131)DNA
L14  (   297214)NUCLEOTIDE
L15  (        6)LIBR?(2W)(DOUBLE STRANDED OR DS)(5W)(DNA OR NUCLEOTIDE)
L16           0 L4 AND LIBR?(2W)(DOUBLE STRANDED OR DS)(5W)(DNA OR NUCLEOTIDE)

=> s l15
          72626 LIBR?
         371243 DOUBLE
          43837 STRANDED
          25378 DOUBLE STRANDED
                   (DOUBLE(W)STRANDED)
          45311 DS
         565131 DNA
         297214 NUCLEOTIDE
L17           6 LIBR?(2W)(DOUBLE STRANDED OR DS)(5W)(DNA OR NUCLEOTIDE)

=> d l17 1-6 ti au so py ab

L17  ANSWER 1 OF 6  CA  COPYRIGHT 2002 ACS
```

L24 ANSWER 5 OF 27 CA COPYRIGHT 2002 ACS
TI Adrenocorticosteroid receptor blockade and excitotoxic challenge regulate adrenocorticosteroid receptor mRNA levels in hippocampus
AU McCullers, Deanna L.; Herman, James P.
SO Journal of Neuroscience Research (2001), 64(3), 277-283
CODEN: JNREDK; ISSN: 0360-4012
PY 2001
AB The mineralocorticoid receptor (MR) and glucocorticoid receptor (GR) are glucocorticoid-**activated transcription factors** essential for maintenance of cellular homeostasis. Differential activation of these adrenocorticosteroid receptors (ACR) is thought to influence neuronal viability, particularly under challenging cellular conditions. The present study is designed to det. the effects of receptor blockade and excitotoxic insult on MR and GR mRNA expression and neuronal viability in hippocampus. Male Sprague-Dawley rats were pretreated for 48 h with vehicle, MR antagonist spironolactone (SPIRO) (50 mg/kg, twice daily, s.c.), or GR antagonist RU486 (25 mg/kg, twice daily, s.c.) and subsequently injected with saline or the glutamate analog kainic acid (KA) (12 mg/kg i.p.). Twenty-four hr post-insult, MR and GR mRNA levels were assessed by in situ **hybridization** anal., and hippocampal neurons were counted to assess KA-induced cell loss. MR blockade with SPIRO increased basal MR mRNA levels in hippocampal subregions CA1, CA3, and dentate gyrus (DG) and increased basal GR mRNA levels in CA3. GR blockade with RU486 increased basal GR mRNA levels in CA3. The excitotoxin KA decreased MR mRNA levels in CA1 and CA3, decreased GR mRNA levels in DG, and negated all antagonist-induced increases of ACR mRNAs. Cell counts quantifying KA damage indicated increased CA3 vulnerability to KA insult after treatment with MR antagonist spironolactone but demonstrated no significant cell loss in any other group or region. These results demonstrate dynamic regulation of hippocampal MR and GR mRNAs after ACR antagonist treatment and kainate toxicity, underscoring the potential importance of MR and GR availability to neuronal viability after insult.

L24 ANSWER 6 OF 27 CA COPYRIGHT 2002 ACS
TI Different regulation of oestrogen receptors .alpha. and .beta. in the human cervix at term pregnancy
AU Wang, Hong; Stjernholm, Ylva; Ekman, Gunvor; Eriksson, Hakan; Sahlin, Lena
SO Molecular Human Reproduction (2001), 7(3), 293-300
CODEN: MHREFD; ISSN: 1360-9947
PY 2001
AB During pregnancy, a cervical connective tissue remodelling takes place, clin. recognized as softening, effacement and dilatation. The role of estrogens and their receptors (ER) in this process is not clear. ER.alpha. is a ligand-**activated transcription factor** involved in many physiol. processes. The identification of a second estrogen receptor, ER.beta., has led to a re-evaluation of estrogen signaling and physiol. The aim of this study was to monitor the expression of the two ERs in the cervix from women at term pregnancy (TP) and after parturition (PP) compared with that of non-pregnant (NP) counterparts. A soln. **hybridization** assay showed that the level of ER.alpha. mRNA was significantly decreased in the PP group, when compared with the NP and TP groups. In contrast the ER.beta. mRNA level was increased in the TP group compared with the NP and PP groups. These results were supported by reverse transcription-polymerase chain reaction (RT-PCR). Similar results were obsd. for the protein with immunohistochem. Intense ER.beta. immunostaining was obsd. in neutrophils and the endothelial cells of blood vessels. In conclusion, this study supports a concept according to which estrogen might be involved in the final remodelling of the cervix via the modulating effects of the two ERs. Furthermore, estrogen may mediate some effects on cervical ripening via ER.beta. present in the invading neutrophils. Further studies are needed to elucidate this finding.

L24 ANSWER 7 OF 27 CA COPYRIGHT 2002 ACS
TI Peroxisome proliferator-activated receptor .alpha. is an androgenresponsive gene in human prostate and is highly expressed in prostatic adenocarcinoma
AU Collett, Gavin P.; Betts, Alan M.; Johnson, Mark I.; Pulimood, Anna B.; Cook, Susan; Neal, David E.; Robson, Craig N.
SO Clinical Cancer Research (2000), 6(8), 3241-3248
CODEN: CCREF4; ISSN: 1078-0432
PY 2000
AB Peroxisome proliferator-activated receptor (PPAR) .alpha. is a member of the nuclear receptor superfamily of ligand-**activated transcription factors**. PPAR.alpha. is activated by peroxisome proliferators and fatty acids and was shown to be involved in the transcriptional regulation of genes involved in fatty acid metab. In rodents, the PPAR.alpha.-mediated change in such genes results in peroxisome proliferation and can lead to the induction of hepatocarcinogenesis. Using the mRNA differential display technique and Northern blot anal., the authors have shown that chronic exposure of the prostate cancer epithelial cell line LNCaP to the synthetic androgen mibolerone results in the down-regulation of PPAR.alpha. mRNA. Levels of PPAR.alpha. mRNA are reduced to approx. 40% of control levels in LNCaP cells exposed to 10 nM mibolerone for 96 h. PPAR.alpha.-responsive reporter plasmids derived from human ApoA-II and muscle carnitine palmitoyl-transferase I genes were stimulated by the PPAR.alpha.-activating ligand Wy-14,643 in LNCaP cells. In situ **hybridization** and immunohistochem. analyses showed that PPAR.alpha. expression in prostate is confined to epithelial cells. In benign prostatic tissue, PPAR.alpha. mRNA was either absent or only weakly expressed in the basal epithelial cells. In 11 of 18 (61%) poorly differentiated (Gleason score, 8-10) prostatic carcinoma specimens, there was strong expression of PPAR.alpha. compared with 4 of 12 Gleason score 7 tumors and 2 of 11 Gleason score 3-6 tumors ($P < 0.01$). These results suggest that PPAR.alpha. is found and functional in human prostate and is down-regulated by androgens. The role of PPAR.alpha. may be to integrate dietary fatty acid and steroid hormone signaling pathways, and its overexpression in advanced prostate cancer may indicate a role in tumor progression with the potential involvement of dietary factors.

L24 ANSWER 8 OF 27 CA COPYRIGHT 2002 ACS
TI A xenobiotic-stress-**activated transcription factor** and its cognate target genes are preferentially expressed in root tip meristems
AU Klinedinst, Susan; Pascuzzi, Pete; Redman, Julia; Desai, Mihir; Arias, Jonathan
SO Plant Molecular Biology (2000), 42(5), 679-688
CODEN: PMBIDB; ISSN: 0167-4412
PY 2000
AB In plants, as-1-type cis elements and their trans-acting factors confer tissue-specific and signal-responsive activities to the promoters of several glutathione S-transferase (GST) genes. Regulation of as-1 is widely thought to involve trans-acting factors that belong to a family of basic/leucine-zipper "TGA factors" that selectively bind this element. The authors have previously shown that TGA1a, a highly conserved TGA factor of tobacco, enhances transcription through as-1 in response to xenobiotic-stress cues. To better understand the functional contribution of this transcription factor to the expression of as-1-regulated genes, the authors have studied its tissue- and cell-specific localization in tobacco seedlings. The authors show here that the relative amt. of TGA1a transcripts expressed in roots and shoots correlate with the as-1-regulated, basal-level expression of a GUS transgene and two putative target GST genes. In situ **hybridization** of intact seedlings demonstrated that TGA1a and these GST genes are preferentially expressed in root tip meristems. Similar findings were made with a gene-specific probe for PG13, a homolog of TGA1a, demonstrating that both factors are

likely to be present in the same root meristem cells. Furthermore, TGA1a protein was immunol. detected exclusively in the primary root and its meristem. Collectively, these studies suggest that TGA1a, and perhaps PG13, may contribute to the expression of GST isoenzymes, esp. in root tip meristems. The biol. significance of these observations is discussed.

L24 ANSWER 9 OF 27 CA COPYRIGHT 2002 ACS
TI Expression of peroxisome proliferator-activated receptor .gamma. (PPAR.gamma.) in human transitional bladder cancer and its role in inducing cell death
AU Guan, You-Fei; Zhang, Ya-Hua; Breyer, Richard M.; Davis, Linda; Breyer, Matthew D.
SO Neoplasia (New York) (1999), 1(4), 330-339
CODEN: NEOPFL; ISSN: 1522-8002
PY 1999
AB The present study examd. the expression and role of the thiazolidinedione (TZD)-**activated transcription factor**, peroxisome proliferator-activated receptor .gamma. (PPAR.gamma.), in human bladder cancers. In situ **hybridization** shows that PPAR.gamma. mRNA is highly expressed in all human transitional epithelial cell cancers (TCCa's) studied (n=11). PPAR.gamma. was also expressed in five TCCa cell lines as detd. by RNase protection assays and immunoblot. Retinoid X receptor .alpha. (RXR.alpha.), a 9-cis-retinoic acid stimulated (9-cis-RA) heterodimeric partner of PPAR.gamma., was also co-expressed in all TCCa tissues and cell lines. Treatment of the T24 bladder cancer cells with the TZD PPAR.gamma. agonist troglitazone, dramatically inhibited 3H-thymidine incorporation and induced cell death. Addn. of the RXR.alpha. ligands, 9-cis-RA or LG100268, sensitized T24 bladder cancer cells to the lethal effect of troglitazone and two other PPAR.gamma. activators, ciglitazone and 15-deoxy-.DELTA.12,14-PGJ2 (15dPGJ2). Troglitazone treatment increased expression of two cyclin-dependent kinase inhibitors, p21WAF1/CIP1 and p16INK4, and reduced cyclin D1 expression, consistent with G1 arrest. Troglitazone also induced an endogenous PPAR.gamma. target gene in T24 cells, adipocyte-type fatty acid binding protein (A-FABP), the expression of which correlates with bladder cancer differentiation. In situ **hybridization** shows that A-FABP expression is localized to normal uroepithelial cells as well as some TCCa's. Taken together, these results demonstrate that PPAR.gamma. is expressed in human TCCa where it may play a role in regulating TCCa differentiation and survival, thereby providing a potential target for therapy of uroepithelial cancers.

L24 ANSWER 10 OF 27 CA COPYRIGHT 2002 ACS
TI Identification of a repressor of estrogen receptor activity, an immunoassay for measuring REA, and use in potentiating the activity of antiestrogen compounds
IN Katzenellenbogen, Benita S.; Montano, Monica M.
SO PCT Int. Appl., 50 pp.
CODEN: PIXXD2
PY 2000
AB The action of nuclear hormone receptors is tripartite, involving the receptor, its ligands, and its coregulator proteins. The estrogen receptor (ER), a member of this superfamily, is a hormone-**activated transcription factor** that mediates the stimulatory effects of estrogens and the inhibitory effects of antiestrogens like tamoxifen in breast cancer and other estrogen target cells. To understand how antiestrogens and dominant neg. ERs suppress ER activity, a dominant neg. ER was used as bait in two-**hybrid** screening assays from which a clone from breast cancer cells was isolated that potentiates the inhibitory activities of dominant neg. ERs and in antiestrogen-liganded ER. At higher concns., it also represses the transcriptional activity of the estradiol-liganded ER, while having no effect on other nuclear hormone receptors. This clone, denoted REA for "repressor of estrogen receptor activity", encodes a 37 kDa protein that

is the first ER-selective coregulator to be identified. Its competitive reversal of steroid receptor coactivator (SRC-1) enhancement of ER activity and its direct interaction with liganded ER indicate that it plays an important role in detg. the sensitivity of estrogen target cells, including breast cancer cells, to antiestrogens and estrogens. The invention provides purified REA, antibody to REA, expression vectors for synthesis of REA in cells transformed by the vector, and labeled REA having an indicator moiety attached thereto or incorporated in its structure. The invention further provides for measuring REA using an immunoassay. Fusion proteins of REA are also claimed as is its use in potentiating the activity of an antiestrogen.

L24 ANSWER 11 OF 27 CA COPYRIGHT 2002 ACS
TI Acute changes in maternal thyroid hormone induce rapid and transient changes in gene expression in fetal rat brain
AU Dowling, Amy L. S.; Martz, Gabriel U.; Leonard, Jack L.; Zoeller, R. Thomas
SO Journal of Neuroscience (2000), 20(6), 2255-2265
CODEN: JNRSDS; ISSN: 0270-6474
PY 2000
AB Despite clin. evidence that thyroid hormone is essential for brain development before birth, effects of thyroid hormone on the fetal brain have been largely unexplored. One mechanism of thyroid hormone action is regulation of gene expression, because thyroid hormone receptors (TRs) are ligand-**activated transcription factors**. We used differential display to identify genes affected by acute T4 administration to the dam before the onset of fetal thyroid function. Eight of the 11 genes that we identified were selectively expressed in brain areas known to contain TRs, indicating that these genes were directly regulated by thyroid hormone. Using in situ **hybridization**, we confirmed that the cortical expression of both neuroendocrine-specific protein (NSP) and Oct-1 was affected by changes in maternal thyroid status. Addnl., we demonstrated that both NSP and Oct-1 were expressed in the adult brain and that their responsiveness to thyroid hormone was retained. These data are the first to identify thyroid hormone-responsive genes in the fetal brain.

L24 ANSWER 12 OF 27 CA COPYRIGHT 2002 ACS
TI The human vitamin D receptor gene (VDR) is localized to region 12cen-q12 by fluorescent in situ **hybridization** and radiation **hybrid** mapping: genetic and physical VDR map
AU Taymans, Susan E.; Pack, Svetlana; Pak, Evgenia; Orban, Zsolt; Barsony, Julia; Zhuang, Zhengping; Stratakis, Constantine A.
SO Journal of Bone and Mineral Research (1999), 14(7), 1163-1166
CODEN: JBMREJ; ISSN: 0884-0431
PY 1999
AB The vitamin D receptor (VDR) is a member of the steroid hormone receptor superfamily of ligand-**activated transcription factors**. The VDR gene was previously mapped to human chromosome 12q13-12q14, but its precise phys. and genetic localization are unknown. The present study reports the mapping of the human VDR gene by radiation **hybrid** (RH) anal., the isolation of a bacterial artificial chromosome (BAC) contg. this gene, and phys. mapping of the VDR gene by fluorescent in situ **hybridization** (FISH). RH anal. placed the VDR gene locus at chromosome 12cen-q12, flanked by Stanford Human Genome Center (SHGC) 30216 and SHGC 9798 (D12S1892) markers. FISH anal. of a BAC contg. the VDR gene confirmed its centromeric location. Thus, the authors have identified a BAC and genetic markers which can be used in the genetic anal. of the VDR gene and investigation of its involvement in osteoporosis and related disorders. The authors conclude that the VDR gene is centromeric to its previously reported locus on chromosome 12.

L24 ANSWER 13 OF 27 CA COPYRIGHT 2002 ACS
TI An estrogen receptor-selective coregulator that potentiates the

effectiveness of antiestrogens and represses the activity of estrogens
AU Montano, Monica M.; Ekena, Kirk; Delage-Mourroux, Regis; Chang, Weiru; Martini, Paolo; Katzenellenbogen, Benita S.
SO Proceedings of the National Academy of Sciences of the United States of America (1999), 96(12), 6947-6952
CODEN: PNASA6; ISSN: 0027-8424
PY 1999
AB The action of nuclear hormone receptors is tripartite, involving the receptor, its ligands, and its coregulator proteins. The estrogen receptor (ER), a member of this superfamily, is a hormone-**activated transcription factor** that mediates the stimulatory effects of estrogens and the inhibitory effects of antiestrogens such as tamoxifen in breast cancer and other estrogen target cells. To understand how antiestrogens and dominant neg. ERs suppress ER activity, we used a dominant neg. ER as bait in two-**hybrid** screening assays from which we isolated a clone from breast cancer cells that potentiates the inhibitory activities of dominant neg. ERs and antiestrogen-liganded ER. At higher concns., it also represses the transcriptional activity of the estradiol-liganded ER, while having no effect on other nuclear hormone receptors. This clone, denoted REA for "repressor of estrogen receptor activity," encodes a 37-kDa protein that is an ER-selective coregulator. Its competitive reversal of steroid receptor coactivator 1 enhancement of ER activity and its direct interaction with liganded ER suggest that it may play an important role in detg. the sensitivity of estrogen target cells, including breast cancer cells, to antiestrogens and estrogens.

L24 ANSWER 14 OF 27 CA COPYRIGHT 2002 ACS
TI Induction of Aryl hydrocarbon Receptor Expression in Embryoblast Cells of Rabbit Preimplantation Blastocysts upon Degeneration of Rauber's Polar Trophoblast
AU Tscheudschilsuren, G.; Kuchenhoff, A.; Klonisch, T.; Tetens, F.; Fischer, B.
SO Toxicology and Applied Pharmacology (1999), 157(2), 125-133
CODEN: TXAPA9; ISSN: 0041-008X
PY 1999
AB The aryl hydrocarbon receptor (AhR) is a ligand-**activated transcription factor** and mediates carcinogenic, teratogenic, and toxic effects of xenobiotics such as dioxin and coplanar polychlorinated biphenyls. The AhR nuclear translocator (ARNT) is involved in AhR signal transduction. We have analyzed the expression of AhR and ARNT mRNA and AhR protein in Day 3 pc (postcoitum) rabbit morulae and Days 4 and 6 pc blastocysts using RT-PCR, nested PCR, whole mount in situ **hybridization**, and whole mount immunohistochem. with subsequent confocal laser scanning anal. AhR and ARNT transcripts were detected in all stages investigated, indicating coexpression of both transcription factors. AhR protein was localized in the cytoplasm. It was detected in Day 3 pc morulae and in blastocysts. In Day 4 pc blastocysts, only trophoblast cells but not embryoblast cells were immunopos. However, at Day 6 pc, the embryoblast cells also expressed AhR protein and this expression was correlated with the degeneration of Rauber's trophoblast layer. (c) 1999 Academic Press.

L24 ANSWER 15 OF 27 CA COPYRIGHT 2002 ACS
TI Retinoid X receptors (RXRs) mRNA expression in human pituitary adenomas
AU Sanno, N.; Sugawara, A.; Tahara, S.; Osamura, R. Y.; Teramoto, A.
SO Endocrine Pathology (1999), 10(1), 73-83
CODEN: ENPAFD; ISSN: 1046-3976
PY 1999
AB Retinoid-X receptors (RXRs) are transcriptional factors that belong to the steroid/thyroid hormone receptor (TR) superfamily. It has been demonstrated that those nuclear receptors act as ligand-**activated transcription factors** in pituitary cells. To det. whether RXRs play roles in the cell differentiation of pituitary adenomas,

we have investigated the expression of RXR.gamma. mRNA in various types of pituitary adenomas using in situ reverse transcriptase-polymerase chain reaction (RT-PCR). The synergistic function on promoters of specific hormones between these nuclear receptors and pituitary specific transcription factor, Pit-1, has been noticed in in vitro expts. The colocalization between RXR.gamma. mRNA and Pit-1 protein was examd. by combined in situ RT-PCR and immunohistochem. RXR.gamma. mRNA was detected in normal pituitary gland as well as all five GH-secreting adenomas and five TSH-secreting adenomas, two of four prolactin (PRL)-secreting adenomas, one of two ACTH-secreting adenomas, one of four nonfunctioning adenomas. By in situ **hybridization** and in situ RT-PCR followed by immunohistochem., the colocalization of Pit-1 mRNA with RXR.gamma. as well as RXR.gamma. mRNA with Pit-1 was obsd. in adenoma cells of GH-secreting adenomas and TSH-secreting adenomas. We suggest that RXR.gamma. may play a role in cell differentiation and hormonal transcription synergistically with Pit-1 in normal and neoplastic human pituitaries.

L24 ANSWER 16 OF 27 CA COPYRIGHT 2002 ACS
TI Expression of Sonic hedgehog, Patched, and Gli1 in developing taste papillae of the mouse
AU Hall, Joshua M.; Hooper, Joan E.; Finger, Thomas E.
SO Journal of Comparative Neurology (1999), 406(2), 143-155
CODEN: JCNEAM; ISSN: 0021-9967
PY 1999
AB Lingual taste buds form within taste papillae, which are specialized structures that develop in a characteristic spatial and temporal pattern. To investigate the signaling events responsible for patterning and morphogenesis of taste papillae, the authors examd. the time course and distribution of expression of several related developmental signaling genes as well as the time course of innervation of taste papillae in mouse embryos from embryonic day 12 (E12) to E18. Lingual expression of the signaling mol. Sonic hedgehog (Shh), its receptor Patched (Ptc), and the Shh-**activated transcription factor** Gli1 were assayed by using in situ **hybridization**. Shh is expressed broadly in the lingual epithelium at E12 but becomes progressively restricted to developing circumvallate and fungiform papillary epithelia. Shh is expressed specifically within the central cells of the papillary epithelium starting at E13.5 and persisting through E18. Ptc and Gli1 expression follow a pattern similar to that of Shh. Compared with Shh, Ptc is expressed in larger regions surrounding the central papillary cells and also in the mesenchyme underlying Shh-expressing epithelium. Innervation of taste papillae was examd. by using the panneuronal antibody to ubiquitin carboxyl terminal hydrolase (protein gene product 9.5). Nerves reach the basal lamina of developing taste papillae at E14 to densely innervate the papillary epithelium by E16. Thus, the pattern of Shh expression within developing taste papillae is established prior to innervation, ruling out neuronal induction of papillae. The results suggest that the Shh signaling pathway may be involved in (1) establishing papillary boundaries in taste papilla morphogenesis, (2) papillary epithelial-mesenchymal interactions, and/or (3) specifying the location or development of taste buds within taste papillae.

L24 ANSWER 17 OF 27 CA COPYRIGHT 2002 ACS
TI Search for Ah (dioxin) receptor target genes which mediate dioxin toxicity. Induction of p27Kip1 cell cycle inhibitor and N-myristoyltransferase 2
AU Kolluri, Siva Kumar
SO Wissenschaftliche Berichte - Forschungszentrum Karlsruhe (1999), FZKA 6201, 1-109 pp.
CODEN: WBFKF5; ISSN: 0947-8620
PY 1999
AB Dioxins, in particular TCDD, are potent mammalian toxins acting predominantly in the thymus and skin, in body wt. regulation and in liver

carcinogenesis. The Ah receptor (AhR) a ligand **activated transcription factor** belonging to the bHLH-PAS protein family mediates the toxicity of dioxins. Despite the extensive research conducted during the past 20 yr, the mechanism by which AhR mediates the toxicity of dioxins is not understood. Known AhR regulated genes mostly code for xenobiotic-metabolizing enzymes but the AhR target gene(s) which mediate toxicity are not known. In this study 5L rat hepatoma cells were employed as a model system for dioxin toxicity in which TCDD severely delays cell cycle progression in the G1 phase by an AhR dependent mechanism. An AhR deficient variant subclone of 5L cells, the BP8 cells, are resistant to TCDD. These AhR-deficient cells were used for a mutational anal. of AhR overexpression to test the required properties of AhR to delay cell cycle progression. Both, the receptor's capacity for sequence specific DNA recognition and the presence of the transcriptional activation domain are necessary to induce the cell cycle delay. This suggests that AhR mediates the TCDD effects on cell cycle by bona fide induction of yet to be identified target genes. Such AhR target genes were searched following two approaches, e.g., based on the biochem. anal. of the cell cycle machinery and by a systematic search for AhR induced genes. Evidence from biochem. anal. of the cell cycle machinery suggested that TCDD might induce cell cycle inhibitor(s). One of the inhibitory proteins, p27Kip1, is induced by TCDD in 5L cells. Induction of p27Kip1 occurs through the direct induction of Kip1 mRNA by AhR. AhR-dependent activation of Kip1-transcription is a novel mechanism of Kip1 induction which is distinct from the accumulation of Kip1 protein caused by posttranscriptional regulation in all the cases reported so far. Kip1 is the cause for TCDD-induced delay of 5L cell proliferation, since inhibition of Kip1 accumulation by expression of antisense RNA almost completely abolishes the effects of TCDD on the cell cycle. The induction of Kip1 could explain some of the toxic effects of TCDD in vivo which are assocd. with reduced proliferation, like the TCDD-induced atrophy of the thymus. Evidence for e role of Kip1 in thymus toxicity of TCDD has been generated in the group by the use of Kip1 deficient mice. In a second approach, suppression subtractive **hybridization** was performed to identify TCDD-induced genes in 5L cells. Among the identified 34 differentially expressed genes, 22 were already known to be induced by TCDD. In addn., there are 3 known genes whose expression was previously not known to be induced by TCDD and 8 novel sequences. A longer cDNA fragment corresponding to one of the clones was isolated and identified as part of the N-myristoyltransferase 2 (NMT-2) gene. TCDD is the 1st substance known to induce NMT-2 transcriptionally. NMT-2 is an enzyme catalyzing myristoylation of many proteins, one of which is the signal transducing Tyr kinase p60Src. NMT-2 mRNA increased in livers of mice treated with TCDD in vivo. Thus NMT-2 may play a role in liver carcinogenicity of dioxins, since increased myristoylation of proteins and, in particular, the Src family protein kinases is implicated in carcinogenesis. In conclusion, the chosen approaches allowed the identification of several novel dioxin-induced target genes of the Ah receptor. One of the induced genes, the p27Kip1 cell cycle inhibitor, was shown to be essentially required for dioxin toxicity in 5L cells. The complexity of changes in gene expression, as indicated by the independent induction of many and not obviously related genes, suggests that dioxins trigger multiple genetically defined response pathways rather than one 'master gene' responsible for all symptoms of dioxin toxicity.

L24 ANSWER 18 OF 27 CA COPYRIGHT 2002 ACS
TI Expression of germ cell nuclear factor (GCNF/RTR) during spermatogenesis
AU Zhang, Yong-Lian; Akmal, Karin M.; Tsuruta, James K.; Shang, Quan; Hirose, Takahisa; Jetten, Anton M.; Kim, Kwan Hee; O'Brien, Deborah A.
SO Molecular Reproduction and Development (1998), 50(1), 93-102
CODEN: MREDEE; ISSN: 1040-452X
PY 1998
AB Germ cell nuclear factor (GCNF/RTR), a novel orphan receptor in the nuclear receptor superfamily of ligand-**activated**

transcription factors, is expressed predominantly in developing germ cells. In several mammalian species two GCNF/RTR mRNAs are present in the testis, with the smaller 2.3-kb transcript generally expressed at higher levels than the larger 7.4- or 8.0-kb transcript. In both the mouse and rat, the 2.3- and 7.4-kb GCNF/RTR transcripts were detected in isolated spermatogenic cells, but not in Sertoli cells. Expression of these transcripts is differentially regulated, with the larger 7.4-kb mRNA appearing earlier during testicular development. The major 2.3-kb transcript is expressed predominantly in round spermatids in the mouse and rat. In situ **hybridization** studies in the rat demonstrated that GCNF/RTR transcripts reach maximal steady-state levels in round spermatids at stages VII and VIII of the spermatogenic cycle, and then decline abruptly as spermatids begin to elongate. RNase protection assays were used to predict the 3' termination site of the 2.3-kb transcript. An alternative polyadenylation signal (AGUAAA) was identified just upstream of this termination site. These studies suggest that GCNF/RTR may regulate transcription during spermatogenesis, particularly in round spermatids just prior to the initiation of nuclear elongation and condensation.

L24 ANSWER 19 OF 27 CA COPYRIGHT 2002 ACS
TI Member of the peroxisome proliferator-activated receptor family of transcription factors is differentially expressed by oligodendrocytes
AU Granneman, James; Skoff, Robert; Yang, Xiaoyi
SO Journal of Neuroscience Research (1998), 51(5), 563-573
CODEN: JNREDK; ISSN: 0360-4012
PY 1998
AB Peroxisome proliferator-activated receptors (PPARs) are ligand-**activated transcription factors** that form a subfamily within the steroid hormone receptor group. Recent work has shown that one member of this group, PPAR.gamma. plays a central role in adipocyte differentiation. As oligodendrocytes are major lipid-producing cells, the authors investigated whether members of the PPAR family were present in oligodendrocytes and whether known PPAR activators affect oligodendrocyte differentiation. Polymerase chain reaction and nuclease protection analyses demonstrated that the principal PPAR present in optic nerve and sciatic nerve is PPAR.delta., whereas adipose tissue expresses mainly PPAR.gamma.. In situ **hybridization** of primary glial cultures revealed PPAR.delta. message in oligodendrocytes but not in astrocytes. PPAR.delta. message was strongly expressed in immature oligodendrocytes, suggesting a role in oligodendrocyte differentiation. Glial cultures contg. immature oligodendrocytes were treated with CP 68,722 and bromopalmitate, compds. known to activate PPARs in adipocytes. These agents increased the no. of oligodendrocytes with membrane sheets three- to fourfold, accelerated the rate of formation of membrane sheets, and increased the size of the membrane sheets. The abundant expression of PPAR.delta. in oligodendrocytes in vivo and in vitro suggests that this PPAR plays a crit. role in oligodendrocyte development and that PPAR activators can be used to manipulate oligodendrocyte maturation in tissue culture.

L24 ANSWER 20 OF 27 CA COPYRIGHT 2002 ACS
TI Expression of peroxisome proliferator-activated receptors in urinary tract of rabbits and humans
AU Guan, Youfei; Zhang, Yahua; Davis, Linda; Breyer, Matthew D.
SO American Journal of Physiology (1997), 273(6, Pt. 2), F1013-F1022
CODEN: AJPHAP; ISSN: 0002-9513
PY 1997
AB Peroxisome proliferator-activated receptors (PPARs, .alpha., .beta./.delta., and .gamma.) are members of the nuclear receptor superfamily of ligand-**activated transcription factors**. PPARs regulate the expression of genes involved in lipid metab. 8(S)-hydroxyeicosatetraenoic acid (8-S-HETE), leukotriene B4 (LTB2), and hypolipidemic fibrates activate PPAr.alpha., whereas

PPAR.gamma. is activated by prostaglandin metabolites. The present studies examd. the intrarenal and tissue distribution of rabbit and human PPAR.alpha., -.beta./.delta., and -.gamma. mRNAs. Nuclease protection showed PPAR.alpha. predominated in liver, heart, and kidney, whereas PPAR.gamma., a putative adipose-specific transcription factor, was in white adipose tissue, bladder, and ileum, followed by kidney and spleen. Lower expression levels of PPAR.beta./.delta. were obsd. in several tissues. In situ **hybridization** of kidney showed PPAR.alpha. mRNA predominated in proximal tubules and medullary thick ascending limbs of both rabbit and human. PPAR.gamma. was exclusively expressed in medullary collecting duct and papillary urothelium. Immunoblot confirmed the expression of PPAR.gamma. protein in freshly isolated inner medullary collecting ducts. MRNAs for all the PPARs were expressed in the ureter and bladder in both rabbit and human, but PPAR.gamma. expression was greatest. This distinct distribution of PPAR isoforms has important implications for lipid-activated gene transcription in urinary epithelia.

L24 ANSWER 21 OF 27 CA COPYRIGHT 2002 ACS
TI Human Ah receptor (AHR) gene: localization to 7p15 and suggestive correlation of polymorphism with CYP1A1 inducibility
AU Micka, Jana; Milatovich, Athena; Menon, Anil; Grabowski, Gregory A.; Puga, Alvaro; Nebert, Daniel W.
SO Pharmacogenetics (1997), 7(2), 95-101
CODEN: PHMCEE; ISSN: 0960-314X
PY 1997
AB The mammalian arom. hydrocarbon receptor (AHR) is a ubiquitous ligand-**activated transcription factor**. AHR ligands include 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD; dioxin), benzo[a]pyrene, and polychlorinated and polybrominated biphenyls; the endogenous ligand is not yet known. Following ligand binding, the AHR transcriptionally activates genes encoding drug-metabolizing enzymes important in both the metabolic potentiation of substrates to genotoxic reactive intermediates and ultimate carcinogens, and the detoxification of toxic or carcinogenic drugs and other environmental pollutants. AHR-mediated gene expression is also involved in many crit. life processes (e.g. cell type-specific differentiation, cell division, apoptosis) by signal transduction mechanisms. Similar to mice, human populations exhibit a >20-fold range of the CYP1A1 inducibility/AHR affinity phenotype. In the present study, the human AHR gene was localized to chromosome 7p15, using fluorescence in situ **hybridization** (FISH). Linkage anal. in a 3-generation family showed with good probability that the high CYP1A1 inducibility phenotype segregates with the 7p15 region. Sequencing 93 nucleotides (31 amino acids) of the human AHR gene's exon 9, which is the region correlated with the mouse A375V polymorphism responsible for the major portion of high vs low CYP1A1 inducibility/AHR affinity, no nucleotide differences were found; Val-381 was present in all 5 individuals examd. (4 related and 1 unrelated), 2 of whom show "high" and 3 of whom show "low" CYP1A1 inducibility. These data indicate that the "high" and "low" CYP1A1 inducibility trait, in the population studied, cannot be explained by a difference among these 31 amino acids in exon 9 of the AHR gene.

L24 ANSWER 22 OF 27 CA COPYRIGHT 2002 ACS
TI Androgens modulate glucocorticoid receptor mRNA, but not mineralocorticoid receptor mRNA levels, in the rat hippocampus
AU Kerr, Janice E.; Beck, Sheryl G.; Handa, Robert J.
SO Journal of Neuroendocrinology (1996), 8(6), 439-447
CODEN: JOUNE2; ISSN: 0953-8194
PY 1996
AB Androgen, mineralocorticoid and glucocorticoid receptors (AR, MR and GR, resp.) are ligand-**activated transcription factors** that alter gene expression and have a wide variety of effects in the central nervous system. High levels of AR, MR and GR mRNA have been found in the CA1 pyramidal cell region of the rat hippocampus

and all 3 of these proteins bind to a similar hormone response element in DNA suggesting the possibility of common receptor function or cross-talk between these receptors at the level of transcription. To begin to investigate this hypothesis, we examd. the regulation of AR, MR and GR mRNA expression in the rat hippocampus following treatment with androgens in combination with gonadectomy and/or adrenalectomy. Three-month-old Sprague-Dawley rats were either castrated for 3 wk, castrated and immediately implanted with 2 Silastic capsules filled with the non-aromatizable androgen, dihydrotestosterone, or left gonadally intact. Four days prior to sacrifice, these animals were either adrenalectomized or sham operated. GR, MR and AR mRNA were measured in the hippocampal subfields using in situ **hybridization**. In the CA1 region, dihydrotestosterone treatment of castrates decreased GR mRNA levels to 69 % of levels found in gonadally intact rats and prevented the adrenalectomy-induced increases in GR mRNA obsd. in gonadally intact and castrated animals. No changes in GR mRNA were obsd. in the CA3 region or dentate gyrus, where AR expression is low or absent. There was no effect of androgen treatment on MR mRNA levels nor did gonadectomy or androgen replacement alter the increases in MR mRNA following adrenalectomy. AR mRNA levels in the CA1 region were unchanged across all treatment groups. In vitro binding studies revealed almost complete nuclear occupancy of hippocampal AR in dihydrotestosterone-treated castrates. No appreciable in vitro binding of dihydrotestosterone to hippocampal MR or GR (Ki.apprxeq.1500 nM) was obsd. which suggests that androgen regulation of GR mRNA in the hippocampus is occurring through AR binding. These data demonstrate a functional similarity of androgens and glucocorticoids in the regulation of GR mRNA levels in an area where AR and GR are colocalized. Androgen-mediated downregulation of GR expression may prove to be an important event in the adaptive responses of CA1 pyramidal cells to hormonal stimuli.

L24 ANSWER 23 OF 27 CA COPYRIGHT 2002 ACS
TI Cytokine regulated mammary gland transcription factor MGF and the gene encoding it
IN Groner, Bernd; Gouilleux, Fabrice; Wakao, Hiroshi
SO Can. Pat. Appl., 41 pp.
CODEN: CPXXEB
PY 1995
1996
AB The mammary gland-specific transcription factor MGFis purified and characterized and a cDNA encoding it is cloned. The transcription factor is a member of an emerging novel family called STATs (Signal Transducers and Activators of Transcription). The gene may be used to manuf. the protein for further the studies or in the development of diagnostics such as **hybridization** probes or antibodies. Methods for using MGF proteins to identify and characterize compds. that affect the intracellular signal transduction of a lactogenic hormone are also described. Ion-exchange and affinity purifn. of sheep MGF is described. A cDNA for the protein was cloned by screening a lactating mammary gland bank with an amino acid sequence-derived probe. Two transcripts of 4.5 and 6.5 kb are found with the smaller the predominant one and it is found in ovary, thymus, spleen, kidney, lung, muscle, adrenal, and in cytotoxic T-cells. A COS cell system in which genes for MDF and the prolactin receptor were expressed was used to show that MGF was activated by the long form of the prolactin receptor. MGF was phosphorylated in vivo.

L24 ANSWER 24 OF 27 CA COPYRIGHT 2002 ACS
TI The dioxin receptor and its nuclear translocator (Arnt) in the rat brain
AU Kainu, Tommi; Gustafsson, Jan-Aake
SO NeuroReport (1995), 6(18), 2557-60
CODEN: NERPEZ; ISSN: 0959-4965
PY 1995
AB Dioxins are environmental pollutants, whose detrimental effects on health are the cause of wide public concern due to their accumulation in the food

chain and resistance to metab. The most well known dioxin is 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). Dioxins exert their effects through a ligand **activated transcription factor** termed the dioxin or aryl hydrocarbon receptor (Ahr), which acts in concert with another structurally related protein: the aryl hydrocarbon nuclear translocator (Arnt). In the present study, the authors have employed in situ **hybridization** to study the localization of the mRNAs for these two proteins in the rat brain. The authors found mRNAs for both Ahr and Arnt predominantly in the same neuronal populations: in the olfactory bulb, the hippocampus, and the cerebral and cerebellar cortices. Arnt, however, had a more widespread expression than Ahr in the brain. The present results demonstrate that dioxins may act directly in the brain and that the effects of dioxin may occur in discrete neuronal populations. However, in some parts of the brain, e.g. the hypothalamus, that are thought to be targets of the toxic effects of dioxins, the authors did not observe detectable levels of Ahr mRNA. Furthermore, it appears that Arnt may have addnl. functions in the brain, apart from being the heterodimerization partner of Ahr, possibly through heterodimerizing with other transcription factors.

L24 ANSWER 25 OF 27 CA COPYRIGHT 2002 ACS
TI Developmental expression of two members of a new class of transcription factors: I. Expression of aryl hydrocarbon receptor in the C57BL/6N mouse embryo
AU Abbott, B.D.; Birnbaum, L.S.; Perdew, G.H.
SO Developmental Dynamics (1995), 204(2), 133-43
CODEN: DEDYEI; ISSN: 1058-8388
PY 1995
AB The aryl hydrocarbon receptor (AhR) is a ligand-**activated transcription factor** with a basic region/helix-loop-helix (bHLH) motif. AhR has been sequenced and the functional domains defined and there is information on the formation of complexes with other peptides and interactions with DNA, although these areas continue to be investigated. AhR mediates many biol. effects such as developmental toxicity, including induction of cleft palate and hydronephrosis. This regulatory protein is expressed in embryonic liver and has been immunohistochem. localized in cells of human and mouse secondary palate. The expression of AhR in embryonic tissues and its ability to disrupt development suggests a significant role for this protein in development. The present study examines the pattern of AhR expression in the C57BL/6N mouse embryo from gestation days (GD) 10-16, using in situ **hybridization** and immunohistochem. anal. AhR mRNA was localized with 35S-RNA antisense riboprobe (cAh1 probe, 1.8 Kb amino terminal DNA). AhR protein was localized with purified monoclonal antibody (RPT-9) raised against the N-terminal peptide sequence. AhR mRNA and protein were expressed in GD 10-13 neuroepithelium, and as development progressed the levels in brain decreased. GD 10-12 embryos also showed AhR in branchial arches, heart, somites, and liver. AhR protein and mRNA in heart were highest at GD 10-11 and decreased with age. In liver, AhR mRNA and protein levels increased and nuclear localization became more pronounced with gestational age. In GD 14-16 embryos levels in liver and adrenal were highest, but AhR was present in ectoderm, bone, and muscle. AhR expression was specific for both cell type, organ/tissue, and developmental stage, suggesting that this novel ligand-activated transcriptional regulator may be important in normal embryonic development.

L24 ANSWER 26 OF 27 CA COPYRIGHT 2002 ACS
TI Chromosomal localization of the human AHR locus encoding the structural gene for the Ah receptor to 7p21.fwdarw.p15
AU Le Beau, M. M.; Carver, L. A.; Espinosa, R. III; Schmidt, J. V.; Bradfield, C. A.
SO Cytogenetics and Cell Genetics (1994), 66(3), 172-6
CODEN: CGCGBR; ISSN: 0301-0171

PY 1994
AB The AHR locus encodes the structural gene for the Ah receptor, a ligand **activated transcription factor** that regulates the expression of a no. of enzymes involved in the metab. of chem. carcinogens and that appears to mediate the tumor promoting properties of compds. such as 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). Using polymerase chain reaction (PCR), the authors amplified exon-10 and intron-D of the AHR gene from human genomic DNA. By using PCR anal. of somatic cell **hybrids** and fluorescence in situ **hybridization** of metaphase cells, the authors localized AHR to human chromosome 7, bands p21.fwdarw.p15. This mapping data should prove useful in detg. the role that the AHR locus plays in human cancer incidence and in the identification of human populations with altered susceptibilities to the toxic/carcinogenic effects of planar arom. hydrocarbons.

L24 ANSWER 27 OF 27 CA COPYRIGHT 2002 ACS
TI Measurement of ligand-induced activation in single viable T cells using the lacZ reporter gene
AU Karttunen, Jaana; Shastri, Nilabh
SO Proceedings of the National Academy of Sciences of the United States of America (1991), 88(9), 3972-6
CODEN: PNASA6; ISSN: 0027-8424
PY 1991
AB The bacterial .beta.-galactosidase gene (lacZ) was used as a reporter gene for the rapid measurement of T-cell antigen receptor (TCR)-mediated activation of individual T cells. The reporter construct contained the lacZ gene under the control of the nuclear factor of activated T cells (NF-AT) element of the human interleukin 2 enhancer. The activity of the intracellular lacZ enzyme was analyzed by flow cytometric measurement of fluorescein accumulation in cells loaded with the fluorogenic .beta.-galactosidase substrate fluorescein di-.beta.-D-galactopyranoside. As a model system, the T-cell **hybridoma** BO4H9.1, which is specific for the lysozyme peptide (amino acids 74-88)/Ab complex, was transfected with the NF-AT-lacZ construct. LacZ activity was induced in 50-100% of the transfectant cells following exposure to pharmacol. agents, to the physiol. peptide/major histocompatibility complex ligand, or to other TCR-specific stimuli. Interestingly, increasing concns. of the stimulus increased the fraction of lacZ+ cells, but not the level of lacZ activity per cell. Even under widely varying levels of stimulus, the level of lacZ activity in individual lacZ+ cells remained within a remarkably narrow range. Thus, TCR-mediated activation can be readily measured in single T cells and, once committed to activation, the level of NF-AT transcriptional activity in individual T cells is independent of the form or concn. of stimulus. This assay is likely to prove useful for the study of early activation events in individual T cells and of TCR ligands.

=> d his

(FILE 'HOME' ENTERED AT 13:44:50 ON 20 NOV 2002)

FILE 'CA' ENTERED AT 13:44:54 ON 20 NOV 2002
L1 430 S ACTIVATED TRANSCRIPTION FACTOR#
L2 388 S L1 NOT 2002/PY
L3 5 S L2 AND LIBR?
L4 383 S L2 NOT L3
L5 0 S L4 AND LIBR?(2W)(DOUBLE STRANDED OR DS)(5W)(DNA OR NUCLEOTIDE
L6 0 S L1 AND BIOLOG?(5W)SAMPLE
L7 0 S L4 AND LIBR?(W)DS(2W)DNA
L8 (72626)S LIBR?
L9 (371243)S DOUBLE
L10 (43837)S STRANDED
L11 (25378)S DOUBLE STRANDED

```
L12 (     45311)S DS
L13 (    565131)S DNA
L14 (    297214)S NUCLEOTIDE
L15 (         6)S LIBR?(2W)(DOUBLE STRANDED OR DS)(5W)(DNA OR NUCLEOTIDE)
L16           0 S L5 STEP
L17           6 S L15
L18           0 S DNA(3W)BIND?(4W)PROTEIN3
L19       12311 S DNA(3W)BIND?(4W)PROTEIN#
L20          14 S L19 AND L4
L21         369 S L4 NOT L20
L22           4 S L21 AND ARRAY
L23         365 S L21 NOT L22
L24          27 S L23 AND HYBRID?
```

```
L2          388 S L1 NOT 2002/PY
L3            5 S L2 AND LIBR?
L4          383 S L2 NOT L3
L5            0 S L4 AND LIBR?(2W)(DOUBLE STRANDED OR DS)(5W)(DNA OR NUCLEOTIDE
L6            0 S L1 AND BIOLOG?(5W)SAMPLE
L7            0 S L4 AND LIBR?(W)DS(2W)DNA
L8  (     72626)S LIBR?
L9  (    371243)S DOUBLE
L10 (     43837)S STRANDED
L11 (     25378)S DOUBLE STRANDED
L12 (     45311)S DS
L13 (    565131)S DNA
L14 (    297214)S NUCLEOTIDE
L15 (         6)S LIBR?(2W)(DOUBLE STRANDED OR DS)(5W)(DNA OR NUCLEOTIDE)
L16           0 S L5 STEP
L17           6 S L15
L18           0 S DNA(3W)BIND?(4W)PROTEIN3
L19       12311 S DNA(3W)BIND?(4W)PROTEIN#
L20          14 S L19 AND L4

=> s l4 not l20
L21         369 L4 NOT L20

=> s l21 and array
         61527 ARRAY
L22          4 L21 AND ARRAY

=> d l22 1-4 ti au so py ab

L22  ANSWER 1 OF 4  CA  COPYRIGHT 2002 ACS
TI   Functional characterization of WT1 binding sites within the human vitamin
     D receptor gene promoter
AU   Lee, Tae Ho; Pelletier, Jerry
SO   Physiological Genomics [online computer file], (2001), 7(2), 187-200
     CODEN: PHGEFP; ISSN: 1094-8341
     URL: http://physiolgenomics.physiology.org/cgi/reprint/7/2/187.pdf
PY   2001
AB   The Wilms' tumor suppressor gene, wt1, encodes a zinc finger transcription
     factor that can regulate gene expression.  It plays an essential role in
     tumorigenesis, kidney differentiation, and urogenital development.  To
     identify WT1 downstream targets, gene expression profiling was conducted
     using a cDNA array hybridization approach.  We confirm here in
     that the human vitamin D receptor (VDR), a ligand-activated
     transcription factor, is a WT1 downstream target.
     Nuclear run on expts. demonstrated that the effect of WT1 on VDR
     expression is at the transcriptional level.  Transient transfection
     assays, deletion mutagenesis, electrophoretic mobility shift assays, and
     chromatin immunopptn. assays suggest that, although WT1 is presented with
     a possibility of three binding sites within the VDR promoter, activation
     of the human VDR gene appears to occur through a single site.  This site
     differs from a previously identified WT1-responsive site in the murine VDR
     promoter (Maurer U, Jehan F, Englert C, Huebinger G, Weidmann E, DeLucas
     HF, and Bergmann L. J Biol. Chem 276: 3727-3732, 2001).  We also show that
     the products of a Denys-Drash syndrome allele of wt1 inhibit WT1-mediated
     transactivation of the human VDR promoter.  Our results indicate that the
     human VDR gene is a down-stream target of WT1 and may be regulated
     differently than its murine counterpart.

L22  ANSWER 2 OF 4  CA  COPYRIGHT 2002 ACS
TI   Retardation of cochlear maturation and impaired hair cell function caused
     by deletion of all known thyroid hormone receptors
AU   Ruesch, Alfons; Ng, Lily; Goodyear, Richard; Oliver, Dominik; Lisoukov,
     Igor; Vennstroem, Bjoern; Richardson, Guy; Kelley, Matthew W.; Forrest,
     Douglas
```

SO Journal of Neuroscience (2001), 21(24), 9792-9800
CODEN: JNRSDS; ISSN: 0270-6474
PY 2001
AB The deafness caused by early onset hypothyroidism indicates that thyroid hormone is essential for the development of hearing. We investigated the underlying roles of the TR.alpha.1 and TR.beta. thyroid hormone receptors in the auditory system using receptor-deficient mice. TR.alpha.1 and TR.beta., which act as hormone-**activated transcription factors**, are encoded by the Thra and Thrb genes, resp., and both are expressed in the developing cochlea. TR.beta. is required for hearing because TR.beta.-deficient (Thrbtm1/tm1) mice have a defective auditory-evoked brainstem response and retarded expression of a potassium current (Ik,f) in the cochlear inner hair cells. Here, we show that although TR.alpha.1 is individually dispensable, TR.alpha.1 and TR.beta. synergistically control an extended **array** of functions in postnatal cochlear development. Compared with Thrbtm1/tm1 mice, the deletion of all TRs in Thratm1/tm1Thrb5m1/tm1 mice produces exacerbated and novel phenotypes, including delayed differentiation of the sensory epithelium, malformation of the tectorial membrane, impairment of electromech. transduction in outer hair cells, and a low endocochlear potential. The induction of IK,f in inner hair cells was not markedly more retarded than in Thrbtm1/tm1 mice, suggesting that this feature of hair cell maturation is primarily TR.beta.-dependent. These results indicate that distinct pathways mediated by TR.beta. alone or by TR.beta. and TR.alpha.1 together facilitate control over an extended range of functions during the maturation of the cochlea.

L22 ANSWER 3 OF 4 CA COPYRIGHT 2002 ACS
TI Thymocyte development in Ah-receptor-deficient mice is refractory to TCDD-inducible changes
AU Hundeiker, C.; Pineau, T.; Cassar, G.; Betensky, R. A.; Gleichmann, E.; Esser, C.
SO International Journal of Immunopharmacology (1999), 21(12), 841-859
CODEN: IJIMDS; ISSN: 0192-0561
PY 1999
AB The aryl hydrocarbon receptor (AhR), a ligand-**activated transcription factor**, is differentially distributed in tissues and abundant in the thymus epithelium. The activated AhR can induce the transcription of an **array** of genes, including genes of cell growth and differentiation. Neither the physiol. function of the AhR nor its putative natural ligand is known. 2,3,7,8-Tetrachlorodibenzo-p-dioxin (TCDD) is a xenobiotic high-affinity activator of the AhR, and appears to be essential for most of the multifold toxic effects of TCDD. Activation of the AhR by even low doses of TCDD results in general immunosuppression and thymus hypoplasia. TCDD exposure interferes with thymocyte development; for instance, it reduces the proliferation rate of the very immature (CD4-CD8- and CD4-CD8+HSA+) thymocytes, leads to preferential emigration of very immature cells, and drastically skews the differentiation of thymocyte subpopulations towards mature CD4-CD8+ .alpha..beta.TCRhigh thymocytes. As shown here, in fetal thymi of AhR-deficient mice, thymocyte differentiation kinetics as defined by CD4 and CD8 surface markers, was comparable to AhR+/+ C57BL/6 mice. Also, the cell emigration characteristics were similar to AhR+/+ mice. These parameters were refractory to TCDD exposure in the AhR-/- mice, but not in the C57BL/6 mice. However, in AhR deficient mice at gestation day 15 more CD4-CD8- immature cells bore high amts. of the (.alpha..beta.-T-cell receptor). Also, fetal thymocyte nos. were significantly lower, as compared to strain C57BL/6. Thus, the AhR is the mediator of thymotoxic effects of TCDD.

L22 ANSWER 4 OF 4 CA COPYRIGHT 2002 ACS
TI Peroxisome proliferator-activated receptors: a family of lipid-**activated transcription factors**
AU Clarke, Steven D.; Thuillier, Philippe; Baillie, Rebecca A.; Sha, Xiaoming

SO American Journal of Clinical Nutrition (1999), 70(4), 566-571
CODEN: AJCNAC; ISSN: 0002-9165
PY 1999
AB A review with 66 refs. Peroxisome proliferator-activated receptors (PPARs) are a family of nuclear transcription factors that belong to the steroid receptor superfamily. This family of PPARs includes PPAR.alpha., PPAR.delta., PPAR.gamma.1, and PPAR.gamma.2. These PPARs are related to the T3 and vitamin D3 receptors and bind to a hexameric direct repeat as a heterodimeric complex with retinoid receptor X.alpha.. PPARs regulate the expression of a wide **array** of genes that encode proteins involved in lipid metab., energy balance, eicosanoid signaling, cell differentiation, and tumorigenesis. A unique feature of these steroid-like receptors is that the physiol. ligands for PPARs appear to be fatty acids from the n-6 and n-3 families and their resp. eicosanoid products. This review describes the characteristics, regulation, and gene targets for PPARs and relates their effects on gene expression to physiol. outcomes that affect lipid and glucose metab., thermogenesis, atherosclerosis, and cell differentiation.

=> d his

(FILE 'HOME' ENTERED AT 13:44:50 ON 20 NOV 2002)

FILE 'CA' ENTERED AT 13:44:54 ON 20 NOV 2002
L1 430 S ACTIVATED TRANSCRIPTION FACTOR#
L2 388 S L1 NOT 2002/PY
L3 5 S L2 AND LIBR?
L4 383 S L2 NOT L3
L5 0 S L4 AND LIBR?(2W)(DOUBLE STRANDED OR DS)(5W)(DNA OR NUCLEOTIDE
L6 0 S L1 AND BIOLOG?(5W)SAMPLE
L7 0 S L4 AND LIBR?(W)DS(2W)DNA
L8 (72626)S LIBR?
L9 (371243)S DOUBLE
L10 (43837)S STRANDED
L11 (25378)S DOUBLE STRANDED
L12 (45311)S DS
L13 (565131)S DNA
L14 (297214)S NUCLEOTIDE
L15 (6)S LIBR?(2W)(DOUBLE STRANDED OR DS)(5W)(DNA OR NUCLEOTIDE)
L16 0 S L5 STEP
L17 6 S L15
L18 0 S DNA(3W)BIND?(4W)PROTEIN3
L19 12311 S DNA(3W)BIND?(4W)PROTEIN#
L20 14 S L19 AND L4
L21 369 S L4 NOT L20
L22 4 S L21 AND ARRAY

=> s l21 not l22
L23 365 L21 NOT L22

=> s l23 and hybrid?
228190 HYBRID?
L24 27 L23 AND HYBRID?

=> d l24 1-27 ti au so py ab

L24 ANSWER 1 OF 27 CA COPYRIGHT 2002 ACS
TI Regulation of gene expression by small molecules in rice
AU Zhang, Shiping; Chen, Lili; Goff, Stephen A.
SO Novartis Foundation Symposium (2001), 236(Rice Biotechnology), 85-96
CODEN: NFSYF7; ISSN: 1528-2511
PY 2001
AB A system for the regulation of gene expression by small mols. in

transgenic rice was developed. This gene switch system consists of two components: (1) a **hybrid** chem. **activated transcription factor**, and (2) a synthetic target promoter. The two elements were transformed into rice suspension cells and transgenic plants were regenerated. A luciferase reporter under control of the gene switch system displayed as high as 10,000-fold inducibility following exposure to the small mol. ligand. The dose-response and induction time-course were detd. Regulated luciferase activity in activated plants decreased one day following removal of ligand and could be reactivated multiple times without apparent cosuppression. Anal. of luciferase activity following ligand application to media surrounding the roots suggests that ligand can be absorbed and transported systemically. In contrast, reporter activation was limited to a small area when ligand was applied directly to the leaf surface. The described gene switch system represents an important tool for situations requiring conditional gene expression in a monocot species.

L24 ANSWER 2 OF 27 CA COPYRIGHT 2002 ACS
TI Tubular NF-.kappa.B and AP-1 activation in human proteinuric renal disease
AU Mezzano, Sergio A.; Barria, Miguel; Droguett, M. Alejandra; Burgos, M. Eugenia; Ardiles, Leopoldo G.; Flores, Claudio; Egido, Jesus
SO Kidney International (2001), 60(4), 1366-1377
CODEN: KDYIA5; ISSN: 0085-2538
PY 2001
AB Nuclear factor-.kappa.B (NF-.kappa.B) and activated protein-1 (AP-1) are transcription factors that regulate many genes involved in the progression of renal disease. Recent data have shown that NF-.kappa.B is activated in tubules and glomeruli in various exptl. models of renal injury. In vitro studies also suggest that proteinuria could be an important NF-.kappa.B activator. The authors therefore approached the idea that NF-.kappa.B may be an indicator of renal damage progression. Paraffin-embedded renal biopsy specimens from 34 patients with intense proteinuria [14 with minimal change disease (MCD) and 20 with idiopathic membranous nephropathy (MN)] and from 7 patients with minimal or no proteinuria (IgA nephropathy) were studied by Southwestern histochem. for the in situ detection of **activated transcription factors** NF-.kappa.B and AP-1. In addn., by immunohistochem., the authors performed staining for the NF-.kappa.B subunits (p50 and p65) and AP-1 subunits (c-fos, c-jun). By immunohistochem. and/or in situ **hybridization**, the expression of some chemokines [monocyte chemoattractant protein-1 (MCP-1), RANTES, osteopontin (OPN)] and profibrogenic cytokines [transforming growth factor-.beta. (TGF-.beta.)], whose genes are regulated by NF-.kappa.B and/or AP-1, were studied further. NF-.kappa.B was detected mainly in the tubules of proteinuric patients, but rarely in nonproteinuric IgA nephropathy (IgAN) patients. In addn., there was a significant relationship between the intensity of proteinuria and NF-.kappa.B activation in MCD ($r = 0.64$, $P = 0.01$) and MN patients ($r = 0.64$, $P < 0.01$). Unexpectedly, patients with MCD had a significantly higher NF-.kappa.B tubular activation than those with MN ($P < 0.01$). To assess whether there was a different compn. of NF-.kappa.B protein components, immunostaining was performed for the NF-.kappa.B subunits p50 and p65. However, no differences were noted between MCD and MN patients. In those patients, there was a lower tubular activation of AP-1 compared with NF-.kappa.B. Moreover, a strong correlation in the expression of both transcription factors was obsd. only in MN ($r = 0.7$, $P = 0.004$). Patients with progressive MN had an overexpression of MCP-1, RANTES, OPN, and TGF-.beta., mainly in the proximal tubules, while no significant expression was found in MCD patients. On the whole, these results show that a tubular overactivation of NF-.kappa.B and AP-1 and a simultaneous up-regulation of certain proinflammatory and profibrogenic genes are markers of progressive renal disease in humans. Increased activation of solely NF-.kappa.B and/or AP-1 may merely indicate the response of tubular renal cells to injury.

L24 ANSWER 3 OF 27 CA COPYRIGHT 2002 ACS
TI The peroxisome proliferator-activated receptor .alpha. regulates amino acid metabolism
AU Kersten, Sander; Mandard, Stephane; Escher, Pascal; Gonzalez, Frank J.; Tafuri, Sherrie; Desvergne, Beatrice; Wahli, Walter
SO FASEB Journal (2001), 15(11), 1971-1978
CODEN: FAJOEC; ISSN: 0892-6638
PY 2001
AB The peroxisome proliferator-activated receptor .alpha. is a ligand-**activated transcription factor** that plays an important role in the regulation of lipid homeostasis. PPAR.alpha. mediates the effects of fibrates, which are potent hypolipidemic drugs, on gene expression. To better understand the biol. effects of fibrates and PPAR.alpha., we searched for genes regulated by PPAR.alpha. using oligonucleotide microarray and subtractive **hybridization**. By comparing liver RNA from wild-type and PPAR.alpha. null mice, it was found that PPAR.alpha. decreases the mRNA expression of enzymes involved in the metab. of amino acids. Further anal. by Northern blot revealed that PPAR.alpha. influences the expression of several genes involved in trans- and deamination of amino acids, and urea synthesis. Direct activation of PPAR.alpha. using the synthetic PPAR.alpha. ligand WY14643 decreased mRNA levels of these genes, suggesting that PPAR.alpha. is directly implicated in the regulation of their expression. Consistent with these data, plasma urea concns. are modulated by PPAR.alpha. in vivo. It is concluded that in addn. to oxidn. of fatty acids, PPARa also regulates metab. of amino acids in liver, indicating that PPAR.alpha. is a key controller of intermediary metab. during fasting.

L24 ANSWER 4 OF 27 CA COPYRIGHT 2002 ACS
TI GABAergic nature of hypothalamic leptin target neurones in the ventromedial arcuate nucleus
AU Ovesjo, M.-L.; Gamstedt, M.; Collin, M.; Meister, B.
SO Journal of Neuroendocrinology (2001), 13(6), 505-516
CODEN: JOUNE2; ISSN: 0953-8194
PY 2001
AB Leptin is an adipose tissue-derived cytokine hormone, which reduces body wt. via interactions with hypothalamic neurons. Leptin receptors capable of activating the JAK-STAT signal transduction pathway are expressed at high levels in the hypothalamus, particularly in the arcuate nucleus. In order to identify the chem. mediators of leptin's action in the hypothalamus, the authors have examd. whether GABA neurons of the hypothalamic arcuate nucleus contain leptin receptors and the leptin-**activated transcription factor** STAT3.
GABAergic neurons, as visualized by antisera to the GABA-synthesizing enzyme glutamic acid decarboxylase (GAD) and GABA, were demonstrated in the ventromedial and ventrolateral parts of the arcuate nucleus. GABA neurons in the ventromedial arcuate nucleus were shown to contain leptin receptor immunoreactivity, as revealed using an antiserum generated to a sequence common to all isoforms of the leptin receptor (Ob-R), as well as an antiserum generated to the C-terminal end of the long leptin receptor (Ob-Rb), and immunoreactivity for the leptin-induced signal transduction mol. STAT3. Ventromedial GABA neurons were also shown to contain neuropeptide Y, whereas ventrolateral proopiomelanocortin-contg. neurons lacked GAD and GABA immunoreactivity. Levels of mRNA for GAD65, GAD67 and the vesicular GABA transporter (VGAT) were analyzed in the arcuate nucleus of leptin-deficient ob/ob mice and lean control mice by in situ **hybridization**. No significant differences in GAD65, GAD67 or VGAT mRNA were detected in the arcuate nucleus of ob/ob mice as compared to lean control mice. The presence of leptin receptor and STAT3 in GABAergic arcuate neurons, but absence of changes in gene transcription for GAD and VGAT mRNA suggests, that leptin does not transcriptionally regulate the expression of proteins involved in GABAergic transmission in arcuate neurons. However, mechanisms other than transcriptional regulation for leptin to influence arcuate GABA neurons may exist.

Previously 6/8/01

TI Molecular cloning and functional analysis of a factor that binds to the proximal promoter of human angiotensinogen
AU Nakajima, Toshiaki; Inoue, Ituro; Cheng, Tong; Lalouel, Jean-Marc
SO Journal of Human Genetics (2002), 47(1), 7-13
CODEN: JHGEFR; ISSN: 1434-5161
PY 2002
AB A significant assocn. has been reported between a common variant in the angiotensinogen gene (AGT), allele T235, and essential hypertension. In subsequent work, it was found that another variant, the presence of an adenine instead of a guanine 6 bp upstream from the initiation site of transcription, was in abs. linkage disequil. with T235. The nucleotide substitution at the -6 position affected the formation of DNA-protein complexes in gel mobility shift assays and the basal transcription of AGT in transactivation expts. We have further examd. the potential impact of this polymorphism on AGT promoter function. In UV crosslinking anal., 150- and 75-kDa proteins bound to the AGT proximal promoter. The possible involvement of factors that bind to GC-rich domains, including Sp1, Sp3, and AP2, was not supported by gel mobility shift assays. Screening an expression **library** with a **double-stranded DNA** segment centered on -6 led to the isolation of cDNA clones encoding the YB1 protein. The specificity of the interaction of YB1 with the proximal promoter of AGT was verified by Southwestern blotting and gel mobility shift assays. In cotransfection expts., YB1 reduced basal AGT promoter activity in a dose-dependent manner. Although these observations suggest a possible role for YB1 in modulating AGT expression, this function is likely to occur in the context of complex interactions involving other nuclear factors. The work illustrates the challenge of developing a mol. understanding of the relationship between common genetic variants and conditions that are only partly caused by them.

L17 ANSWER 2 OF 6 CA COPYRIGHT 2002 ACS
TI Preparation of normalized cDNA libraries using biotin-labeled DNA/RNA for use in DNA microarray
IN Takagaki, Kazuchika; Kaminishi, Yoshinori
SO PCT Int. Appl., 36 pp.
CODEN: PIXXD2
PY 2002
AB A method of prepg. normalized cDNA library construction using biotinylated DNA or RNA, and use in DNA microarray is described. Single-stranded cDNA **libraries** and biotinylated **double-stranded DNA** or biotinylated RNA are prepd. from double-stranded cDNA libraries and hybridized to each other. Unhybridized circular ssDNA are collected and made into dsDNA. Construction of normalized cDNA libraries from rat liver and human prostate is described.

L17 ANSWER 3 OF 6 CA COPYRIGHT 2002 ACS
TI In vitro selection of aptamers from RNA libraries
AU Kenan, Daniel J.; Keene, Jack D.
SO Methods in Molecular Biology (Totowa, New Jersey) (1999), 118(RNA-Protein Interaction Protocols), 217-231
CODEN: MMBIED; ISSN: 1064-3745
PY 1999
AB Methods for selection of RNA ligands from a randomized RNA library are described, together with the necessary reagents. The protocol proceeds in three phases: (1) conversion of **library** oligonucleotides into **double-stranded DNA** transcription templates; (2) transcription of RNA and multiple cycles of binding, partitioning, amplification, and retranscription; and (3) cloning selected RNAs as double-stranded cDNA into an appropriate vector for downstream studies such as sequencing and target binding. These protocols are fit for using any protein or other org. mol., as well as whole cells, in the selection procedure. A variety of immobilized surfaces such as plastic, nitrocellulose, or antibodies bound to Staph A beads are amenable to these methods.

L17 ANSWER 4 OF 6 CA COPYRIGHT 2002 ACS
TI Full-length cDNA cloning and determination of mRNA 5' and 3' ends by amplification of adaptor-ligated cDNA
AU Chenchik, A.; Diachenko, L.; Moqadam, F.; Tarabykin, V.; Lukyanov, S.; Siebert, P. D.
SO BioTechniques (1996), 21(3), 526-534
CODEN: BTNQDO; ISSN: 0736-6205
PY 1996
AB An efficient cDNA amplification procedure is described for detg. of the 5' and 3' ends of mRNAs and cloning full-length cDNAs. In this approach, a double-stranded (ds) adaptor is ligated to both ends of a **library** of **ds** cDNA by T4 **DNA** ligase. This adaptor-ligated ds cDNA is then used to selectively amplify 5'- or 3'- cDNA fragments by PCR with a combination of gene-specific and adaptor-specific primers. This is a unified method for 5' and 3' rapid amplification of cDNA ends (RACE) from the same adaptor-ligated ds cDNA template. A specially designed adaptor combines features of "vectorette PCR" and "suppression PCR" technologies that significantly reduce background during amplification. The application of "long and accurate PCR" (LA PCR) technol. makes possible the amplification of large RACE products and full-length cDNAs with high fidelity to the original mRNA. We investigated efficacy and limitations of this PCR-based approach for cDNA cloning by amplification of 5'- and 3'-RACE fragments and full-length cDNAs of three members of the abundant human actin gene family (1.3-1.9 kb), the medium abundance transferrin receptor mRNA (5.0 kb) and the low-medium abundance insulin-line growth factor II receptor mRNA (9.1 kb).

L17 ANSWER 5 OF 6 CA COPYRIGHT 2002 ACS
TI The orphan receptor Rev-ErbA.alpha. activates transcription via a novel response element
AU Harding, Heather P.; Lazar, Mitchell A.
SO Molecular and Cellular Biology (1993), 13(5), 3113-21
CODEN: MCEBD4; ISSN: 0270-7306
PY 1993
AB Rev-ErbA.alpha. (Rev-Erb) is a nuclear hormone receptor-related protein encoded on the opposite strand of the .alpha.-thyroid hormone receptor (TR) gene. This unusual genomic arrangement may have a regulatory role, but the conservation of human and rodent Rev-Erb amino acid sequences suggests that the protein itself has an important function, potentially as a sequence-specific transcriptional regulator. However, despite its relationship to the TR, Rev-Erb bound poorly to TR binding sites. To det. its DNA-binding specificity in an unbiased manner, Rev-Erb was synthesized in Escherichia coli, purified, and used to select specific binding sites from **libraries** of random **double-stranded DNA** sequences. Rev-Erb binds to a unique site consisting of a specific 5-bp A-T-rich sequence adjacent to a TR half-site. Rev-Erb contacts this entire asym. 11-bp sequence, which is the longest nonrepetitive element specifically recognized by a member of the thyroid/steroid hormone receptor superfamily, and mutations in either the A/T-rich or TR half-site regions abolished specific binding. The binding specificity of wild-type Rev-Erb was nearly identical to that of C- and N-terminally truncated forms. This binding was not enhanced by retinoid X receptor, TR, or other nuclear proteins, none of which formed heterodimers with Rev-Erb. Rev-Erb also appeared to bind to the selected site as a monomer. Furthermore, Rev-Erb activates transcription through this binding site even in the absence of exogenous ligand. Thus, Rev-Erb is a transcriptional activator whose properties differ dramatically from those of classical nuclear hormone receptors, including the TR encoded on the opposite strand of the same genomic locus.

L17 ANSWER 6 OF 6 CA COPYRIGHT 2002 ACS
TI Nucleotide sequence of a putative transcription factor recognizing the thyroglobulin promoter

AU Javaux, Francoise; Vassart, Gilbert; Christophe, Daniel
SO Nucleic Acids Research (1990), 18(5), 1301
    CODEN: NARHAD; ISSN: 0305-1048
PY 1990
AB The cDNA for a putative transcription factor was isolated from a dog thyroid cDNA expression library. Screening of the **library** with a **double-stranded DNA** fragment of the bovine thyroglobulin promoter, extending from -126 to -107 bp from the transcription start site identified a phage harboring an 1100 bp insert. The specificity of the binding of the recombinant protein to the thyroglobulin promoter sequence was assayed in competition expts. involving unrelated fragments. A complete clone was obtained by rescreening the library with the 1100 bp insert. The full-length sequence is 2264 bp long and encodes an open-reading frame of 1713 bp preceded by a short coding region (216 bp).

```
=> d his

     (FILE 'HOME' ENTERED AT 13:44:50 ON 20 NOV 2002)

     FILE 'CA' ENTERED AT 13:44:54 ON 20 NOV 2002
L1           430 S ACTIVATED TRANSCRIPTION FACTOR#
L2           388 S L1 NOT 2002/PY
L3             5 S L2 AND LIBR?
L4           383 S L2 NOT L3
L5             0 S L4 AND LIBR?(2W)(DOUBLE STRANDED OR DS)(5W)(DNA OR NUCLEOTIDE
L6             0 S L1 AND BIOLOG?(5W)SAMPLE
L7             0 S L4 AND LIBR?(W)DS(2W)DNA
L8   (     72626)S LIBR?
L9   (    371243)S DOUBLE
L10  (     43837)S STRANDED
L11  (     25378)S DOUBLE STRANDED
L12  (     45311)S DS
L13  (    565131)S DNA
L14  (    297214)S NUCLEOTIDE
L15  (         6)S LIBR?(2W)(DOUBLE STRANDED OR DS)(5W)(DNA OR NUCLEOTIDE)
L16            0 S L5 STEP
L17            6 S L15

=> s DNA(3w)bind?(4w)protein3
        565131 DNA
        924261 BIND?
             9 PROTEIN3
L18          0 DNA(3W)BIND?(4W)PROTEIN3

=> s DNA(3w)bind?(4w)protein)
UNMATCHED RIGHT PARENTHESIS 'PROTEIN)'
The number of right parentheses in a query must be equal to the
number of left parentheses.

=> s DNA(3w)bind?(4w)protein#
        565131 DNA
        924261 BIND?
       1638206 PROTEIN#
L19      12311 DNA(3W)BIND?(4W)PROTEIN#

=> s l19 and l4
L20         14 L19 AND L4

=> d l20 1-14 ti au so py ab

L20  ANSWER 1 OF 14  CA  COPYRIGHT 2002 ACS
TI   Transcriptional activation of genes by 17.beta.-estradiol through estrogen
```

receptor-Sp1 interactions
AU Safe, Stephen
SO Vitamins and Hormones (San Diego, CA, United States) (2001), 62, 231-252
CODEN: VIHOAQ; ISSN: 0083-6729
PY 2001
AB This review fucused on 17.beta.-estradiol gene activation through estrogen receptor-Sp1 interactions. Estrogen receptor-.alpha. (ER.alpha.) is a ligand-**activated transcription factor** and a member of the nuclear receptor superfamily. The classic mechanism of ER.alpha. action is assocd. with estrogen-induced formation of a nuclear ER.alpha. homodimer, binding to 5'-regulatory estrogen response elements (EREs) in target gene promoters, interaction with other nuclear proteins, and general transcription factors to activate gene expression. ER.alpha. also interacts with Sp1 protein to transactivate genes through binding Sp1(N)xERE or Sp1(N)xERE half-site (1/2) motifs where both ER.alpha. and Sp1 bind DNA elements. Activation through Sp1 (N)xERE 1/2 requires interactions of both proteins with their cognate DNA elements as well as addnl. nuclear factors to form a functional ER.alpha./Sp1-DNA complex. Recent studies also show that ER.alpha. and Sp1 phys. interact and ER.alpha. preferentially binds to the C-terminal **DNA-binding** domain of Sp1 **protein**. Moreover, ER.alpha./Sp1 can activate transcription from a consensus GC-rich Sp1 binding site in transient transfection studies in MCF-7 human breast cancer cells, and this response is also obsd. with ER.alpha. variants that do not contain the DNA-binding domain. Several genes that are induced by estrogens in MCF-7 cells are activated through one or more GC-rich sites in their regulatory regions and these include the cathepsin D, E2F1, bcl-2, c-fos, adenosine deaminase, insulinlike growth factor binding protein 4, and retinoic acid receptor .alpha.1 genes. ER.alpha./Sp1 and ER.beta./Sp1 action is dependent on ligand structure and cell context and ER.beta./Sp1 is primarily assocd. with decreased ligand-dependent gene expression. ER.alpha./Sp1,. Like ER.alpha./AP1, represents a pathway for hormone activation of genes in which the receptor does not bind DNA, and results of ongoing studies suggest that ER.alpha./Sp1 plays an important role in transcriptional activation of multiple growth regulatory genes in breast cancer cells. (c) 2001 Academic Press.

L20 ANSWER 2 OF 14 CA COPYRIGHT 2002 ACS
TI Ribozyme-mediated cleavage of the estrogen receptor messenger RNA and inhibition of receptor function in target cells
AU Lavrovsky, Yan; Tyagi, Rakesh K.; Chen, Shuo; Song, Chung S.; Chatterjee, Bandana; Roy, Arun K.
SO Molecular Endocrinology (1999), 13(6), 925-934
CODEN: MOENEN; ISSN: 0888-8809
PY 1999
AB Estrogen receptor (ER) functions as a ligand-**activated transcription factor** for estrogen-regulated genes. Because of the crit. role of the ER in the proliferation of certain estrogen-dependent cancer cell types such as the mammary tumor, inhibitors of estrogen action at the level of receptor function are of major clin. interest. Here the authors describe developments of two ribozymes that can selectively degrade the human ER mRNA and inhibit trans-activation of an artificial promoter contg. the estrogen response element. Two ribozymes, designated RZ-1 and RZ-2, cleave the human ER.alpha. mRNA at nucleotide positions +956 and +889, resp. These cleavage sites lie within the coding sequence for the **DNA-binding** domain of the receptor **protein**. Both RZ-1 and RZ-2 were also effective in inhibiting the progression of quiescent MCF-7 breast cancer cells to the S phase of the cell cycle after their exposure to 17 .beta.-estradiol (10-9M). These results provide a new avenue for inhibition of estrogen action by selective mRNA degrdn. with its potential therapeutic application through targeted gene delivery vectors.

L20 ANSWER 3 OF 14 CA COPYRIGHT 2002 ACS

TI Nuclear receptors and their interactions with hormonally active agents in food

AU Gustafsson, Jan-Ake

SO Hormonally Active Agents in Food, Symposium, Kaiserslautern, Germany, Oct. 6-9, 1996 (1998), Meeting Date 1996, 53-61. Editor(s): Eisenbrand, Gerhard. Publisher: Wiley-VCH Verlag GmbH, Weinheim, Germany. CODEN: 67JEAC

PY 1998

AB A review, with 13 refs. Ligand **activated transcription factors** constitute an important mode of regulation of gene expression. Well known examples are the steroid hormone receptors or nuclear receptors which encompass a rapidly growing supergene family of transcription factors activated both by well characterized ligands but also by as yet unknown activators. During recent years much has been learned about the mechanism of action of these **DNA-binding proteins** and a significant amt. of current research efforts in the field center on elucidation of the complicated events taking place after the receptor has bound to DNA and when it signals to the basal transcriptional machinery via a plethora of coactivators and corepressors, the exact interrelationships of which are not yet fully understood. Some environmental toxicants would seem to exert their effects by mimicking natural ligands of these nuclear receptors, thereby inadvertently triggering the cellular responses normally only elicited by physiol. stimuli. For instance, environmental contaminants have been shown to interact with both the androgen receptor and the estrogen receptor and there is reason to believe that harmful effects in human beings can result from these events. The understanding of interactions between environmental toxicants and the estrogen receptor has changed considerably in view of a recent discovery of a novel estrogen receptor which the authors have named estrogen receptor .beta. (ER.beta.), the already known receptor being termed estrogen receptor .alpha.. Pertaining to the characteristics and tissue distribution of ER.beta. will be discussed. Another sol. receptor belonging to a different gene family has since long been in the focus of interest for the understanding of mechanisms of action of such environmental contaminants as dioxin, dibenzofurans and polychlorinated biphenyls, mediated by the Ah receptor, also called the TCDD receptor or dioxin receptor. This species belongs to the so-called bHLH PAS domain family of transcription factors which also encompasses proteins like Arnt, HIF-1.alpha., Sim as well as trachealess. Other addns. to this family are expected in the near future. Just as the nuclear receptor supergene family (cf. above) contains many so-called orphan receptors with unknown activators, many bHLH PAS domain factors also seem to be regulated by low mol. compds., the nature of which is not yet understood. 2,3,7,8-Tetrachlorodibenzoparadioxin inadvertently interacts with the dioxin receptor, probably by resembling a physiol. ligand, and thereby elicits and exaggerates (if dioxin acts as an agonist) or prevents (if dioxin acts as an antagonist) a physiol. response and this may be harmful to the individual. It cannot be excluded that also other members of the bHLH PAS domain family of transcription factors may be targets of environmental toxicants. In addn., both nuclear receptors and bHLH PAS domain transcription factors can be activated by normal constituents in the authors' food. For instance, plant derived dietary components as coumestrol and genistein, so-called phytoestrogens, appear to act as weak agonists on the estrogen receptor and these effects have been suggested to result in some kind of protective influence against development of cancer in tissues such as the breast and the prostate. Interestingly, the novel ER.beta. appears to bind some phytoestrogens more avidly than ER.alpha.. Furthermore, also the Ah receptor appears to interact with plant derived components. Several years ago the authors showed that indolocarbazoles which are formed in the body from indole-3-carbinol constitute high affinity ligands for the Ah receptor and such interactions may have physiol. consequences. In summary, there are multiple examples of environmental impact on ligand **activated transcription factors** and it is conceivable that many

more examples will be found whereby compds. of environmental origin, both physiol. components of the authors' food and potentially harmful man made environmental pollutants, impact upon the activity of important transcription factors leading to potentially far reaching effects on networks of genes and their expression.

L20 ANSWER 4 OF 14 CA COPYRIGHT 2002 ACS
TI A novel cellular site-specific **DNA-binding protein** cooperates with the viral NS1 polypeptide to initiate parvovirus DNA replication
AU Christensen, Jesper; Cotmore, Susan F.; Tattersall, Peter
SO Journal of Virology (1997), 71(2), 1405-1416
CODEN: JOVIAM; ISSN: 0022-538X
PY 1997
AB Replication of linear single-stranded parvovirus DNA proceeds by a rolling-hairpin mechanism which generates long, palindromic, duplex concatemers. Processing to monomer length requires initiation from origins of DNA replication located at the 3' and 5' ends of each embedded monomer, reactions which can be recapitulated in vitro for minute virus of mice (MVM). To det. which cellular proteins were essential for replication from these origins, S100 exts. from 293S cells were fractionated on phosphocellulose. When recombined, these fractions were able to support replication in vitro, dependent on the viral initiator protein NS1, using plasmid forms of the 5' origin or the minimal 3' origin as templates. Fraction P-cell 1 contains two factors, replication protein A (RPA) and proliferating cell nuclear antigen (PCNA), known to be essential for simian virus 40 replication in vitro. When P-cell 1 was replaced with purified recombinant RPA and PCNA, NS1-mediated MVM replication initiated from the 5' origin but not from the 3' origin. The 3' origin is a 50-bp sequence contg. three distinct recognition elements, an NS1 binding site, a site at which NS1 nicks the DNA to generate the priming 3' OH, and a region contg. a consensus **activated transcription factor** (ATF) binding site. To identify the missing factor(s) for 3' origin replication, P-cell 1 was fractionated by further chromatog. and active fractions were identified by their ability to complement RPA, PCNA, and P-cell 2 for NS1-mediated, origin-specific replication. Gel shift and UV crosslinking anal. of the replication-competent fractions revealed a novel 110-kDa sequence-specific **DNA binding protein** which recognized the consensus ATF binding site region of the origin and which we have termed parvovirus initiation factor, or PIF. Binding of PIF appears to activate the endonuclease function of NS1, allowing efficient and specific nicking of the 3' minimal origin under stringent conditions in vitro.

L20 ANSWER 5 OF 14 CA COPYRIGHT 2002 ACS
TI ISGF3.gamma. p48, a specificity switch for interferon **activated transcription factors**
AU Bluyssen, Hans A. R.; Durbin, Joan E.; Levy, David E.
SO Cytokine & Growth Factor Reviews (1996), 7(1), 11-17
CODEN: CGFRFB; ISSN: 1359-6101
PY 1996
AB A review with 54 refs. Interferon (IFN) induces a gene expression by phosphorylating latent transcription factors of the STAT family. Two different STAT multimeric complexes that bind distinct enhancer elements are activated by IFN.alpha. and IFN.gamma., dictated by the **DNA-binding protein** ISGF3.gamma. p48. This protein, a member of the IFN regulatory factor (IRF) family, acts as an adaptor protein to redirect STAT multimers from their intrinsic palindromic sequence specificity to interactions with a composite element composed of an IRF site juxtaposed with a STAT half-site. Sequence similarity within the IRF family suggests that other members could serve as adapter proteins for transcriptional activators. Recent evidence that PIP (LSIRF) sequesters the Ets protein PU.1 at a composite DNA element lends support to this adaptor hypothesis.

L20 ANSWER 6 OF 14 CA COPYRIGHT 2002 ACS
TI Activation of gene transcription by IL-4, IL-13 and IFN-.gamma. through a shared DNA binding motif
AU Koehler, I.; Alliger, P.; Rieber, E. P.
SO Behring Institute Mitteilungen (1995), 96, 78-86
CODEN: BHIMA2; ISSN: 0301-0457
PY 1995
AB Both interleukin-4 (IL-4) and interleukin-13 (IL-13) induce the transcription factor NF-IL4 (nuclear factor IL-4) which preexists in an inactive form and binds to an IL-4 responsive element (IL-4RE) in the promoter regions of IL-4/IL-13-dependent genes. UV-crosslinking and SDS gel electrophoresis indicate that NF-IL4 consists of at least two DNA-binding components of 50 kDa and 100-130 kDa. The IL-4 responsive element is also recognized by an interferon-.gamma. (IFN-.gamma.)-induced **DNA binding protein** for which a Mr of 50 kDa has been detd. A common DNA binding motif for different transcription factors might provide the basis for the frequently obsd. functional antagonism between IL-4/IL-13 and IFN-.gamma.. The activation of transcription factors by IL-4/IL-13 and IFN-.gamma. could be blocked by inhibitors of tyrosine kinases and ser/thr phosphatases but not by a PKC inhibitor, suggesting related signal transduction pathways for these cytokines.

L20 ANSWER 7 OF 14 CA COPYRIGHT 2002 ACS
TI Detection of a novel transcription factor for the A.alpha. fibrinogen gene in response to interleukin-6
AU Liu, Zhiyong; Fuller, Gerald M.
SO Journal of Biological Chemistry (1995), 270(13), 7580-6
CODEN: JBCHA3; ISSN: 0021-9258
PY 1995
AB The three fibrinogen genes belong to the class II hepatic acute phase proteins that are regulated in part by members of the interleukin-6 (IL-6) family of cytokines and glucocorticoids. The common DNA sequence that characterizes this group of proteins is a hexanucleotide CTGGGA residing in the promoter regions of these genes. Investigations of IL-6 control of the A.alpha. fibrinogen gene by electrophoretic mobility shift assays using a 30-base pair DNA probe contg. the CTGGGA element revealed that a novel protein is assocd. with this site during non-IL-6-stimulated conditions. Sensitive time-course studies of IL-6 stimulation using primary hepatocyte cultures, high resoln. polyacrylamide gel electrophoresis, and site-directed mutagenesis show that upon IL-6 stimulation of hepatocytes, this **DNA binding protein** transiently leaves the CTGGGA site and binds 12 base pairs down-stream but then begins to re-assoc. with the original DNA site at 1 h and is completed by 2 h. A recently characterized and cloned IL-6-**activated transcription factor**, Stat-3, which has been reported to bind a CTGGGAA site in the .alpha.-2 macroglobulin gene, another member of the class II acute phase proteins, does not bind to the CTGGGA sequence in the A.alpha. fibrinogen gene. These findings reveal the presence of a previously undefined IL-6-regulated event, which involves a new **DNA binding protein** and demonstrates for the first time addnl. details of the kinetics of IL-6 control of fibrinogen gene expression.

L20 ANSWER 8 OF 14 CA COPYRIGHT 2002 ACS
TI **DNA** sequences that **bind** transcription regulating **proteins** activated in response to various cytokines and their uses
IN Levy, David E.
SO PCT Int. Appl., 48 pp.
CODEN: PIXXD2
PY 1995
1995
1997

1997

AB Oligonucleotides contg. the DNA sequence TTTCCNGGAAA (single- or double-stranded) or their derivs. bind transcriptional regulatory proteins induced by cytokines, growth factors or hormones. Such oligonucleotides are useful in detecting, identifying or purifying transcription regulating proteins. DNA constructs contg. this oligonucleotide sequence linked to a promoter and a reporter gene and cells carrying them are also disclosed. **DNA-binding proteins** other than p91 that are inducible by a cytokine, growth factor or hormone, and that bind to this sequence when tyrosine phosphorylated are described.

L20 ANSWER 9 OF 14 CA COPYRIGHT 2002 ACS

TI Concerted participation of NF-.kappa.B and C/EBP heteromer in lipopolysaccharide induction of serum amyloid A gene expression in liver

AU Ray, Alpana; Hannink, Mark; Ray, Bimal K.

SO Journal of Biological Chemistry (1995), 270(13), 7365-74
CODEN: JBCHA3; ISSN: 0021-9258

PY 1995

AB The promoter region of the rabbit serum amyloid A (SAA) gene contains two adjacent C/EBP and one NF-.kappa.B binding element. Involvement of these elements in SA gene induction, following lipopolysaccharide (LPS) stimulation of the liver, has been studied by investigating LPS-**activated transcription factors** and their interaction with the promoter elements of the SAA gene. Appearance of complexes in the electrophoretic mobility shift assay has indicated that the **DNA-binding proteins** that interact with the NF-.kappa.B element of the SAA promoter are induced in the LPS-treated rabbit liver. Presence of RelA (p65 subunit of NF-.kappa.B) in these complexes was demonstrated by the ability of RelA-specific antisera to supershift the DNA-protein complexes. LPS also induced several members of the C/EBP family of transcription factors, which interaction with the C/EBP motifs of the SAA promoter. Activated C/EBP and RElA form a RelA.cntdot.C/EBP heteromeric complex that assocs. with varying affinity to NF-.kappa.B and C/EBP elements of the SAA gene. Transfection assays using both transcription factor genes have demonstrated that the heteromeric complex of NF-.kappa.B and C/EBP is a much more potent transactivator of SAA expression than each transcription factor alone. The heteromeric complex efficiently promotes transcription from both NF-.kappa.B and C/EBP sites.

L20 ANSWER 10 OF 14 CA COPYRIGHT 2002 ACS

TI Mediation of growth hormone-dependent transcriptional activation by mammary gland factor/Stat 5

AU Wood, Timothy J. J.; Sliva, Daniel; Lobie, Peter E.; Pircher, Tony J.; Gouilleux, Fabrice; Wakao, Hiroshi; Gustafsson, Jan-Ake; Groner, Bernd; Norstedt, Gunnar; Haldosen, Lars-Arne

SO Journal of Biological Chemistry (1995), 270(16), 9448-53
CODEN: JBCHA3; ISSN: 0021-9258

PY 1995

AB Previous observations have shown that binding of GH to its receptor leads to activation of transcription factors via a mechanism involving phosphorylation on tyrosine residues. To establish whether the prolactin-**activated transcription factor** Stat 5 (mammary gland factor) is also activated by GH, nuclear exts. were prepd. from COS-7 cells transiently expressing transfected Stat 5 and growth hormone receptor cDNA. Gel electrophoresis mobility shift analyses revealed the growth hormone-dependent presence of specific **DNA-binding proteins** in these exts. The complexes formed could be supershifted by polyclonal anti-Stat 5 antiserum. In other expts. nuclear exts. from GH-treated Chinese hamster ovary cells stably expressing transfected GH receptor cDNA and liver from GH-treated hypophysectomized rats were used for gel electrophoresis mobility shift analyses. These also revealed the presence of specific **DNA-binding proteins** sharing antigenic determinants with

Stat 5. Stat 5 cDNA was shown to be capable of complementing the GH-dependent activation of transcription of a reporter gene in the otherwise unresponsive COS-7 cell line. This complementation was dependent on the presence of Stat 5 tyrosine 694, suggesting a role for phosphorylation of this residue in GH-dependent activation of DNA-binding and transcription.

L20 ANSWER 11 OF 14 CA COPYRIGHT 2002 ACS
TI Cloning of the Ah-receptor cDNA reveals a distinctive ligand-**activated transcription factor**
AU Burbach, Kristine M.; Poland, Alan; Bradfield, Christopher A.
SO Proceedings of the National Academy of Sciences of the United States of America (1992), 89(17), 8185-9
CODEN: PNASA6; ISSN: 0027-8424
PY 1992
AB A cDNA encoding the murine Ah receptor (Ahb-1 allele for arom. hydrocarbon responsiveness) has been isolated and characterized. Anal. of the deduced protein sequence revealed a region with similarity to the basic region/helix-loop-helix (BR/HLH) motif found in many transcription factors that undergo dimerization for function. In addn. to the BR/HLH domain, the N-terminal domain of the Ah receptor has extensive sequence similarity to the human ARNT (aryl hydrocarbon receptor nuclear translocator) protein and two regulatory proteins of Drosophila, Sim and Per. Photoaffinity labeling and peptide mapping studies indicate that the Ah receptor binds agonist at a domain that lies within this conserved N-terminal domain. The Ah receptor appears to be a ligand-**activated transcription factor** with a helix-loop-helix motif similar to those found in a variety of **DNA-binding proteins**, including Myc and MyoD.

L20 ANSWER 12 OF 14 CA COPYRIGHT 2002 ACS
TI Characterization of downstream elements in a Raf-1 pathway
AU Liaw, G.-J.; Steingrimsson, E.; Pignoni, F.; Courey, A. J.; Lengyel, J. A.
SO Proceedings of the National Academy of Sciences of the United States of America (1993), 90(3), 858-62
CODEN: PNASA6; ISSN: 0027-8424
PY 1993
AB At the poles of the Drosophila embryo, cell fate is established by a pathway that begins with the activation of a membrane-assocd. tyrosine kinase (the torso gene product); this then leads to activation of a serine/threonine kinase (Drosophila Raf-1). Activated Raf-1 then leads, by an undefined mechanism, to the transcriptional activation of the tailless (tll) gene; the tll gene product, itself a transcription factor, subsequently regulates the expression of an array of target genes. To further define this pathway, the authors have utilized sequence comparison between Drosophila melanogaster and Drosophila virilis to identify conserved elements in the tll promoter region. As assessed by DNase I footprinting and promoter dissection expts., two of these elements are potential regulatory targets of Raf-1-**activated transcription factors**. Sequence comparison also reveals that the unique residues in the **DNA-binding** domain of the tll **protein**, the next component in the pathway, are conserved. One of these residues, the alanine after the last cysteine in the first zinc finger, may be responsible for part of the difference between the tll protein DNA binding site and the closely related half-site of the retinoid/estrogen receptors. Consistent with the rapid turnover of the tll protein, it contains a PEST sequence (rich in proline, glutamate and aspartate, serine, and threonine) that is also conserved.

L20 ANSWER 13 OF 14 CA COPYRIGHT 2002 ACS
TI Isolation of a metal-**activated transcription factor** gene from Candida glabrata by complementation in Saccharomyces cerevisiae
AU Zhou, Pengbo; Thiele, Dennis J.

SO Proceedings of the National Academy of Sciences of the United States of America (1991), 88(14), 6112-16
CODEN: PNASA6; ISSN: 0027-8424
PY 1991
AB Metal-inducible transcription of metallothionein (MT) genes involves the interaction of metal-responsive trans-acting factors with specific promoter DNA sequence elements. In this report, a genetic selection using the bakers' yeast, S. cerevisiae, to clone a gene from C. glabrata encoding a metal-activated **DNA-binding protein** denoted AMT is presented. This selection is based on the ability of the AMT1 gene product to activate expression of the C. glabrata MT-I gene in a copper-sensitive S. cerevisiae host strain. **DNA-binding** studies using AMT1 **protein** expressed in Escherichia coli demonstrate that AMT1 is activated by copper or silver to bind to both the MT-I and MT-II promoters of C. glabrata. Sequence comparison of AMT1 protein to the S. cerevisiae copper- or silver-activated **DNA-binding protein**, ACE1, indicates that AMT1 contains the 11 amino terminal cysteine residues known to be crit. for the metal-activated DNA-binding activity of ACE1. In contrast, the carboxyl-terminated portion of AMT1 bears only slight similarity at the primary structure level to the same region of ACE1 known to be important for transcriptional activation. These results suggest that the amino-terminal cysteines, and other conserved residues, play an important role in the ability of AMT1 and ACE1 to sense intracellular copper levels and assume a metal-activated DNA-binding structure.

L20 ANSWER 14 OF 14 CA COPYRIGHT 2002 ACS
TI Transformation of glucocorticoid receptors bound to the antagonist RU 486: effects of alkaline phosphatase
AU Gruol, Donald J.; Wolfe, Kristal A.
SO Biochemistry (1990), 29(34), 7958-66
CODEN: BICHAW; ISSN: 0006-2960
PY 1990
AB RU 486 is a synthetic steroid that binds avidly to glucocorticoid receptors without promoting their transformation into **activated transcription factors**. A significant part of this behavior is due to a failure of the RU 486-bound receptor to be efficiently released from a large (sedimenting at 8-9S) multimeric complex contg. the 90-kilodalton heat-shock protein. In vitro at 15.degree. the RU 486 receptor was slowly released from the 8-9S complex and converted into a **DNA-binding protein** by a process that could be blocked by NaF. Moreover, this transition was accelerated by treatment with alk. phosphatase. High-resoln. anion-exchange chromatog. showed that the profile of receptor subspecies released from the 8-9S complex (in the absence of phosphatase treatment) was different for the RU 486 bound receptor when compared to the receptor occupied by the agonist triamcinolone acetonide. Prodn. of the earliest eluting receptor form (peak A) was inhibited with RU 486. Peak A had previously been shown to be the predominant form of the receptor possessing a capacity to bind DNA. Treatment of the RU 486-receptor complex with alk. phosphatase increase the formation of the peak A subspecies as well as the capacity of receptor to bind DNA-cellulose. Evidently, phosphorylation of the receptor or a tightly bound factor contributes to defining the capacity with which individual steroids can promote dissocn. of the 8-9S complex and conversion of the glucocorticoid receptor into a **DNA-binding protein**.

=> d his

(FILE 'HOME' ENTERED AT 13:44:50 ON 20 NOV 2002)

FILE 'CA' ENTERED AT 13:44:54 ON 20 NOV 2002
L1 430 S ACTIVATED TRANSCRIPTION FACTOR#